UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P O Box 1450
Alexandria, Virginia 22313-1450
www uspto gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/777,470	02/11/2004	Abraham Phillip Lee	703538.4033	2234

34313 7590 04/10/2008
ORRICK, HERRINGTON & SUTCLIFFE, LLP
IP PROSECUTION DEPARTMENT
4 PARK PLAZA
SUITE 1600
IRVINE, CA 92614-2558

EXAMINER	
MUI, CHRISTINE T	

ART UNIT	PAPER NUMBER
1797	

MAIL DATE	DELIVERY MODE
04/10/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/777,470	LEE ET AL.	
	Examiner	Art Unit	
	CHRISTINE T. MUI	1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20 and 31-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20 and 31-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.

4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

5) ☐ Notice of Informal Patent Application

6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

1. The affidavit filed on 31 January 2008 under 37 CFR 1.131 has been considered but is ineffective to overcome the WO 02/068104 to Higuchi reference.

2. The affidavit that was filed on 31 January 2008 is ineffective because it is not signed by both inventors.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000.

Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

2. Claims 1-5 and 13-14 are rejected under 35 U.S.C. 102(b) as being anticipated by CA 2 304 644 to Klinksiek et al (herein referred Klinksiek).

3. CA 2 304 644 has the publication date of April 1999 is also published as DE 198 14 267 published March 1998 and WO 99/15263 published April 1998. The basis of the rejection is made off of the English Translation of WO 99/15263.

4. Regarding claim 1, the reference Klinksiek discloses a device for the preparation of a silicone, silane or silicone/silane emulsion composed of a silicone containing and/or silane-containing active substance component and an aqueous phase with a first mixing station for the emulsion components fed via pumps P1, P2, P3 from storage tanks. The process prepared fine particles of aqueous silicone and/or silane emulsions with narrow particle size distribution (see page 4, lines 16-23 and 29-30).

5. Regarding claims 2-4, the reference Klinksiek discloses in Figure 1, a possible embodiment of the device may include a silicone oil being injected into the aqueous phase via a first nozzle and immediately afterwards is mixed intensively and homogenized in the second nozzle. A final dispersion then takes place in the downstream jet disperser. The emulsifier present that coats the surface of the particles can have certain silicone active substances, that may be modified in such a way that operations are carried out with deficient amount of water containing the entire quantity of emulsifier (see page 6, lines 21-26, page 7, lines 8-19). It is known in the art that oil

and water are immiscible solutions and it is interpreted by the examiner that the solutions with active silicone substance can be solvents to make an emulsion.

6. Regarding claim 5, the reference Klinksiek discloses that it is known in the art to prepare a fine particle and stable silicone emulsion of oil in water. Prior to homogenization, silicon is introduced slowly with stirring into an aqueous emulsifier mixture before the resulting coarse-particle emulsion undergoes actual homogenization (see page 1, lines 3-5 and 12-14).

7. Regarding claim 13, the reference Klinksiek discloses that it is known in the art to stir in silicon particles into an aqueous solution (see page 1, lines 12-14).

8. Regarding claim 14, the reference Klinksiek discloses the nozzle arrangements are preferably fed by means of two pumps with pressure difference of 2-3 bar in such a way where the coating speed of the emulsifier permits the aqueous emulsifier solution and the silicone are fed together in the final emulsion concentration and homogenized directly by means of the jet disperser in one or a maximum of three passes. With the present pressure of the nozzles, the particles may have sizes of <1 mm with emulsifier contents in the region of 0.5-3% (see page 6, line 28-page 7, line 2, see page 8, lines 13-18). It is interpreted by the examiner that where there is a pressure difference between the nozzles that feeds the oil or aqueous phases can be changed or altered or be a large difference that the shear force is created that is large enough to overcome the interfacial forces to form an emulsion with a coating to produce particles of a desired size.

9. Claims 1-4, 7 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 02/068104 to Higuchi (submitted on the Information Disclosure Statement on 10 September 2004, herein referred "Higuchi").

10. WO 02/068104 has an English equivalent US Pub. No. 2006/0079585. All rejections are based off of the English equivalent translation 2006/0079585.

11. Regarding claim 1, the reference Higuchi discloses a process and apparatus for rapidly producing an emulsion and microcapsules in a simple manner. The microcapsules include a step of feeding a shell-forming phase to a continuous phase. A dispersion phase is ejected toward the junction of the flow of a first and second continuous phase flowing in the microchannels. The dispersion phase joins the flows of the first and second continuous phase and produces a microdroplet (see Figure 6, abstract, page 1 [0007], page 4 [0060-0061]).

12. Regarding claims 2-4, the reference Higuchi discloses that the flows used in the apparatus in the continuous phase can be oil and the dispersion phase can be water (see page 3 [0055]). It is known in the art that oil and water are immiscible solutions.

13. Regarding claim 7, the reference Higuchi discloses that the continuous phase is a solution of oil containing 70% oleic acid (see page 3 [0053]). It is known in the art that oleic acid is an amphiphilic molecule.

14. Regarding claim 14, the reference Higuchi discloses that microdroplets with a specific size of 25 μm can be obtained when the pressure of the dispersion phase is set to 2.45 kPa and the continuous phase is set to 4.85 kPa. When the pressure changes in the continuous phase, changes the diameter of the microdroplets produced can be

altered (see page 3 [0053]). It is interpreted by the examiner that an increase in pressure of the phases, the greater the shear force is created, overcoming interfacial forces of another stream.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

17. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

18. Claims 6-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Klinksiek.

19. Regarding claim 6, the reference Klinksiek discloses the claimed invention except for specifically adding reagent to the aqueous solution is a drug. Klinksiek teaches that it is known in the art to slowly stir in silicon particles into an aqueous solution (see page 1, lines 12-14). It would have been obvious to one having ordinary skill in the art at the time the invention was made to add a drug reagent instead of silicon particles to the aqueous solution to produce microparticles with a drug rather than silicone.

20. Regarding claim 7, the reference Klinksiek discloses the claimed invention except for specifically disclosing dissolving a first type of amphiphilic molecule in the second solution. Klinksiek discloses that the aqueous phase may contain an emulsifier that contains silicon active substances. The amount of emulsifier may be modified in such a way that operations are carried out with any deficient amount of water that may contain the entire quantity of emulsifier (see page 6, line 28-page 7, line 19). It is interpreted by the examiner that the emulsifier is a type of amphiphilic molecule in an aqueous solution. It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the content of the aqueous phase by adding an emulsifier that displays both hydrophobic and hydrophilic properties.

21. Claims 8-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Klinksiek as applied to claim 1 above, and further in view of Handa et al. (herein referred "Handa").

22. Regarding claims 8-9, the reference Klinksiek discloses the claimed invention except for producing a mono- and bi- layer vesicle with an amphiphilic molecule. Handa discloses a method for producing a phospholipid monolayer at the triolein saline interface that is converted into a bilayer through differential quenching of N-dansyl-PE (see abstract and page 2888, left column, Formation of Microemulsion). It would have been obvious to one having ordinary skill in that art at the time the invention was made to produce a monolayer vesicle and convert it into a bilayer vesicle in order to determine the stability of the monolayer and to examine the properties of the bilayer in the pharmaceutical, chemical or medicine fields.

23. Regarding claims 10-11, the reference Klinksiek discloses the claimed invention except for using different types of amphiphilic molecules in the production of the vesicles. Handa discloses that in experimentation, the interfacial tensions of phospholipids include phosphatidylcholine, phosphatidylethanolamine and phosphatidylserine, in the triolein saline emulsion (see abstract). It would have been obvious to one having ordinary skill in that art at the time the invention was made to examine different amphiphilic molecules to determine the stability and interfacial tension of the monolayers of each lipid for purposes of testing in pharmaceutical, chemicals or medicines.

24. Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Klinksiek and Handa as applied to claim 9 above.

25. Regarding claim 12, the reference Klinksiek and Handa disclose the claimed invention except for the first and second solution interface is formed by a third solution flowing downstream through two downstream input channels. Klinksiek discloses a device for producing silicon and/or siliane emulsions where a silicone oil is injected into the aqueous phase via a nozzle and is immediately afterwards mixed intensively and homogenized in a second nozzle. A final fine dispersion takes place in the downstream jet disperser (see page 6, lines 21-30, Figure 6). The device in Figure 6 is capable of having an inlet stream moved downstream to allow a microdroplet from the first two streams and then a new microdroplet from a third inlet stream. It would have been obvious to one having ordinary skill in that art at the time the invention was made to construct the microchannels in a way where the inlet steams are joined together to produce a bilayer vesicle where the two inlets are joined immediately and a third is joined downstream to allow time to form the first monolayer vesicle.

26. Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Klinksiek as applied to claim 14.

27. Regarding claim 15, the reference Klinksiek discloses the claimed invention but does not explicitly disclose increasing the flow rates of the second and third stream. Klinksiek discloses the pressure difference between the nozzles can be between 2-3 bare where the coating permits the aqueous emulsifier solution and the silicone are fed

together in the final emulsion concentration (see page 6, line 28-page 7, line 2). It would have been obvious to one having ordinary skill in the art at the time the invention was made to increase the flow rate of the nozzles into the jet disperser to have different flow rates of the second and third stream to change the size of the particles produced when homogenized and to ensure the desired final emulsion concentration is reached upon mixing of the phases.

28. Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Klinksiek as applied to claim 1 above, and further in view of Nisisako et al. (submitted on the Information Disclosure Statement on 10 September 2004, herein referred "Nisisako").

29. Regarding claim 16, the reference Klinksiek discloses the claimed invention except for controlling flow rates of the three inlet streams. Nisisako teaches that it is known in the art to prepare microdroplets inside a liquid layer at a T-junction in a microchannel network and observing the flow speed (average velocity) and the droplet size in the continuous phases (see page 958, section 3.1). It would have been obvious to one having ordinary skill in the art at the time the invention was made to alter the continuous phase and dispersion phase flow rates of the microchannel set up either it be a T-junction or a set up with three microchannels comprising of two continuous phases and one dispersion phase to observe the change in droplet size produced in relation to the flow rates.

30. Claims 17–20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Klinksiek and Nisisako as applied to claim 13 above.

31. Regarding claim 17, the reference Klinksiek and Nisisako disclose the claimed invention except for the flow rates being controlled by one or more pumps. Klinksiek teaches that it is known in the art to produce a silicone emulsion that is delivered by pumps with different pressure differences (see page 6, line 28-29). It would have been obvious to one having ordinary skill in the art at the time the invention was made to use pumps to deliver a continuous stream of pressure to the microchannels to produce microdroplets.

32. Regarding claim 18, the reference Klinksiek discloses the claimed invention except for manipulating the flow rate of the first solution to control the rate of the droplet formation. Nisisako teaches that it is known to change the flow speed of the continuous phase to change the droplet size. The droplet size decrease as the average velocity increases of the continuous phase (see page 958, section 3.1). It would have been obvious to one having ordinary skill in that art at the time the invention was made to change the flow rate of the dispersion phase with an aqueous solution to change the size of the droplet, rather than the continuous phase flow rate.

33. Regarding claims 19-20, the reference Klinksiek discloses the claimed invention except for increasing the flow rate of the second solution to decrease the size of the droplets formed. Nisisako teaches that it is known in the art that at a given dispersed phase, the droplet size decreases as the average velocity (flow speed) increase of the continuous phase flow (see page 958, section 3.1 and Figure 3). In Figure 3, the graph

shows the effect on the droplet size of the continuous phase flow, either increasing or decreasing. As the size of the droplet decreases, the continuous phase flow speed increases. The continuous phase flow content was high and oleic sunflower oil was used as the oil phase. It would have been obvious to one having ordinary skill in the art at the time the invention was made to change the flow speed of the continuous phase flow at a constant dispersed phase to change the droplet size produced.

34. Claims 31-33 is rejected under 35 U.S.C. 103(a) as being unpatentable over Klinksiek, and further in view of USP 6,211,654 to Quake (herein referred "Quake").

35. Regarding claim 31, the reference Klinksiek discloses a process and apparatus for rapidly producing an emulsion and microcapsules in a simple manner. The microcapsules include a step of feeding a shell-forming phase to a continuous phase. A dispersion phase is ejected toward the junction of the flow of a first and second continuous phase flowing in the microchannels. The dispersion phase joins the flows of the first and second continuous phase and produces a microdroplet (see Figure 6, abstract, page 1 [0007], page 4 [0060-0061]). Quake discloses a device for analyzing and sorting polynucleotides by size (see abstract and column 1, line 14-17). It would have been obvious to one having ordinary skill in the art at the time the invention was made to produce a microdroplet from the sandwiching of three streams and process the droplet formed for analyzing purposes.

36. Regarding claims 32-33, the reference Klinksiek discloses the claimed invention except for processing the droplet generated from the first stream. Quake discloses a microfabricated device for analyzing and sorting the polynucleotide by size (see abstract and column 1, line 14-17). It would have been obvious to one having ordinary skill in the art at the time the invention was made to produce microdroplets by sheath flow then analyze and sort the particles by size to determine different sizes produced from the sandwiching of three input streams.

37. Claims 34-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Klinksiek and Quake as applied to claim 31 above, and further in view of USP 6,733,172 to Lee (herein referred "Lee").

38. Regarding claims 34-36, the references Klinksiek and Quake disclose the claimed invention except for splitting the droplets into equal or unequal sizes. Lee discloses a magnetohydrodynamic fluidic system that splits droplets in a MHD microfluidic channel (see column 5, lines 65-66). An initial droplet in the droplet splitter channel is moved along the microfluidic channel by utilizing a sequential set of MHD pumps. The pumps provide a MHD micropump in which the Lorentz force is used to propel the droplet along the microchannel. The droplet is stretched into separate droplets by control of the MHD pumps that are selectively activated to stretch the droplet until the components are separate (see column 6, lines 1-6 and 21-31). Since the controls are selectively activated the droplet splitter is capable of producing equal and unequal sized droplets by activating particular pumps to stretch and separate the

components. It would have been obvious to one having ordinary skill in the art at the time the invention was made to split a droplet into smaller components for minuscule sampling or testing of droplets.

39. Regarding claim 37, the reference Klinksiek and Quake disclose the claimed invention except for the processing comprises of fusing two or more droplets together. Lee discloses a droplet mixer where one droplet is stretched into two component sections and a second droplet is moved into contact with the droplet and by use of MHD pumps the two droplets are combine to form a mixed material (see column 6, lines 43-56, Figure 3A-B). It would have been obvious to one having ordinary skill in the art at the time the invention was made to fuse two droplets together to form a larger droplet either mixing materials or creating a larger droplet for analysis.

40. Claims 34-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Klinksiek and Quake as applied to claim 31 above, and further in view of WO 2004/002327 to Stone et al. (submitted on the Information Disclosure Statement on 10 September 2004, herein referred "Stone").

41. Regarding claims 34-36, the references Klinksiek and Quake disclose the claimed invention except for splitting the droplets into equal and unequal sizes. Stone discloses a microfluidic device and method for forming a discontinuous section of similar or dissimilar size in a fluid provided (see abstract). In a plurality of microchannels, each carrying a plurality of subject droplet are moved along the channel toward a different arrangement of obstruction to form a variety of different sized droplets. As the droplet

flows through the channel, it is free from obstruction and its flow is unaffected. In the different channels, depending on the arrangement of the obstructions, the sizes of the new droplets downstream of the obstructions can be of equal/uniform size or unequal sizes. This occurs when the larger droplet comes in contact with the obstruction(s) (see page 19, lines 15-33; Figure 6). It would have been obvious to one having ordinary skill in the art at the time the invention was made to incorporate obstructions in different patterns in the outlet channels of the newly formed microdroplet emulsions to split or form discontinuous sections of similar or dissimilar fluid particles.

42. Claim 38 is rejected under 35 U.S.C. 103(a) as being unpatentable over Klinksiek, and further in view of USP 6,540,895 to Spence (herein referred “Spence”).

43. Regarding claim 38, the reference Klinksiek discloses a device for producing a silicone and/or silane emulsion where the components are fed by the means of two pumps, one for the two aqueous phases and one for the silicone oil. The dispersion of the emulsion that is formed is dispersed in a downstream jet (see page 6, lines 21-29). It is interpreted by the examiner that the three input channels are the two aqueous phase channels and the one silicone oil channel. The junction is where all three streams meet and are fed together to form a final emulsion concentration is mixed. Spence discloses a microfacricated device for sorting cells based on a desired characteristic such as reporter labeled cells and can be sorted by the presence or level of the reporter on the cell. Along the main channel of the sample inlet there is a detection region that is in communication with processor (computers and software) to

detect a signal representative of cell characteristics (see abstract and column 8, lines 27-29 and 36-37). It would have been obvious to one having ordinary skill in the art at the time the invention was made to use a detection system that detects cell characteristics with a computer, where data can be stored and processed, to be used in the analysis of microdroplets that are produced from the multiple input microchannels with the aid of pumps.

44. Claim 39 is rejected under 35 U.S.C. 103(a) as being unpatentable over Klinksiek as applied to claim 38 above, and further in view of Lee and USP 2002/0058332 to Quake and Thorsen (submitted on the Information Disclosure Statement on 10 September 2004, herein referred "Thorsen").

45. The reference Klinksiek discloses the claimed invention except for where the droplet splitter has two or more daughter channels in communication with the splitter input channel. Thorsen discloses a microfluidic device for analyzing and/or sorting biological materials with a main channel and branch channels (see page 8 [0077]). Lee discloses a device where there are MHD pumps located along the microchannels that are capable of moving the droplet in the microchannel to the desired location or splitting the droplet (see column 6, lines 21-24 and Figure 2B). It would have been obvious to one having ordinary skill in that art at the time the invention was made to combine the microfluidic device of Thorsen and the MHD pumps of Lee along the walls of the microchannels to move the droplets to desired locations along the channels and split

the droplet at the precise location to allow each split droplet flow down each daughter/branch channel.

46. Claim 40 is rejected under 35 U.S.C. 103(a) as being unpatentable over Klinksiek as applied to claim 38 above, and further in view of Quake.

47. Regarding claim 40, the reference Klinksiek discloses the claimed invention except for droplet processor that comprises of droplet sorter. Quake discloses a microfabricated device that analyzes and sorts single polynucleotides by size. The device has a solution inlet that has a plurality of branch channels that are in fluid communication and branch out from the discrimination region. The flow of molecules is maintained through the device via a pump of pressure differential and a directing means comprising of a valve structure at the branch point effective to permit the molecule to enter only one of the branches (see column 2, lines 49-51, 63-67, column 7, line 8, 14-20 and Figure 1). It would have been obvious to one having ordinary skill in that art at the time the invention was made to sort the droplets that are formed via an input channel and daughter channels that are regulated via pumps to maintain a flow and a pressure gradient to avoid the droplets in the device from being stagnant.

48. Claim 41 is rejected under 35 U.S.C. 103(a) as being unpatentable over Klinksiek and Quake as applied to claim 38 above, and further in view of Lee.

49. Regarding claim 41, the references Klinksiek and Quake disclose the claimed invention except for the droplet processor comprises of a droplet fuser. Lee discloses a magnetohydrodynamic fluidic system that mixes droplets. The droplet mixer disclosed

is enhanced by stretching one droplet to engulf another. A first droplet is introduced into a microchannel and moved along the channel by a set a MHD pumps and stretched into two separate component sections. A second droplet is introduced into another microchannel and moved toward the first stretched droplet by use of the MHD pumps and moved into contact with the first droplet between the two separate component sections of the droplet. The set of MHD pumps are used to combine the droplet to form a mixed material (see column 6, lines 43-56; Figures 3A-B). It would have been obvious to one having ordinary skill in the art at the time the invention was made to fuse together two microparticles in a device to form a larger particle with either different or identical concentrations to produce a well-mixed particle for analysis.

50. Claims 5-6 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Higuchi as applied to claim 1 above, and further in view of Klinksiek.

51. Regarding claim 5, the reference Higuchi discloses the claimed invention except for dissolving a reagent in the first solution. Klinksiek teaches that it is known in the art to prepare a fine particle and stable silicone emulsion of oil in water. Prior to homogenization, silicon is introduced slowly with stirring into an aqueous emulsifier mixture before the resulting coarse-particle emulsion undergoes actual homogenization (see page 1, lines 3-5 and 12-14). It would have been obvious to one having ordinary skill in the art at the time the invention was made to dissolve a reagent in the aqueous solution to create a mixture for the water phase before emulsion to produce a microparticle with a composition of interest.

52. Regarding claim 6, the reference Higuchi discloses the claimed invention except for where the added reagent to the aqueous solution is a drug. Klinksiek teaches that it is known in the art to slowly stir in silicon particles into an aqueous solution (see page 1, lines 12-14). It would have been obvious to one having ordinary skill in the art at the time the invention was made to add a drug reagent instead of silicon particles to the aqueous solution to produce microparticles with a drug rather than silicone.

53. Regarding claim 13, the reference Higuchi discloses the claimed invention except for where a polymer molecule is dissolved in the second solution. Klinksiek teaches that it is known in the art to stir in silicon particles into an aqueous solution (see page 1, lines 12-14). It would have been obvious to one having ordinary skill in that art at the time the invention was made to add a polymer to the second solution as there was silicon mixed into an aqueous solution to create a silicone and/or silane emulsion to change the content of the microdroplet formed after a collision of the continuous and dispersion phases.

54. Claims 8-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Higuchi as applied to claim 1 above, and further in view of Handa et al. (herein referred "Handa").

55. Regarding claims 8-9, the reference Higuchi discloses the claimed invention except for producing a mono- and bi- layer vesicle with an amphiphilic molecule. Handa discloses a method for producing a phospholipid monolayer at the triolein saline interface that is converted into a bilayer through differential quenching of N-dansyl-PE

(see abstract and page 2888, left column, Formation of Microemulsion). It would have been obvious to one having ordinary skill in that art at the time the invention was made to produce a monolayer vesicle and convert it into a bilayer vesicle in order to determine the stability of the monolayer and to examine the properties of the bilayer in the pharmaceutical, chemical or medicine fields.

56. Regarding claims 10-11, the reference Higuchi discloses the claimed invention except for using different types of amphiphilic molecules in the production of the vesicles. Handa discloses that in experimentation, the interfacial tensions of phospholipids include phosphatidylcholine, phosphatidylethanolamine and phosphatidylserine, in the triolein saline emulsion (see abstract). It would have been obvious to one having ordinary skill in that art at the time the invention was made to examine different amphiphilic molecules to determine the stability and interfacial tension of the monolayers of each lipid for purposes of testing in pharmaceutical, chemicals or medicines.

57. Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Higuchi and Handa as applied to claim 9 above, and further in view of Klinksiek.

58. The reference Higuchi and Handa disclose the claimed invention except for the first and second solution interface is formed by a third solution flowing downstream through two downstream input channels. Klinksiek discloses a device for producing silicon and/or siliane emulsions where a silicone oil is injected into the aqueous phase via a nozzle and is immediately afterwards mixed intensively and homogenized in a

second nozzle. A final fine dispersion takes place in the downstream jet disperser (see page 6, lines 21-30, Figure 6). The device in Figure 6 is capable of having an inlet stream moved downstream to allow a microdroplet from the first two streams and then a new microdroplet from a third inlet stream. It would have been obvious to one having ordinary skill in that art at the time the invention was made to construct the microchannels in a way where the inlet steams are joined together to produce a bilayer vesicle where the two inlets are joined immediately and a third is joined downstream to allow time to form the first monolayer vesicle.

59. Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Higuchi as applied to claim 14.

60. Regarding claim 15, the reference Higuchi discloses the claimed invention but does not explicitly disclose increasing the flow rates of the second and third stream. Higuchi discloses changing the pressure of the dispersion and continuous phases to alter the size of the microdroplets, and it would have been obvious to one having ordinary skill in the art at the time the invention was made to alter the flow rates of the continuous phases to alter the microdroplet sizes while changing the pressures of the phases.

61. Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Higuchi as applied to claim 1 above, and further in view of Nisisako et al. (submitted on the Information Disclosure Statement on 10 September 2004, herein referred “Nisisako”).

62. Regarding claim 16, the reference Higuchi discloses the claimed invention except for controlling flow rates of the three inlet streams. Nisisako teaches that it is known in the art to prepare microdroplets inside a liquid layer at a T-junction in a microchannel network and observing the flow speed (average velocity) and the droplet size in the continuous phases (see page 958, section 3.1). It would have been obvious to one having ordinary skill in the art at the time the invention was made to alter the continuous phase and dispersion phase flow rates of the microchannel set up either it be a T-junction or a set up with three microchannels comprising of two continuous phases and one dispersion phase to observe the change in droplet size produced in relation to the flow rates.

63. Claims 17–20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Higuchi and Nisisako as applied to claim 13 above, and further in view of Klinksiek.

64. Regarding claim 17, the reference Higuchi and Nisisako disclose the claimed invention except for the flow rates being controlled by one or more pumps. Klinksiek teaches that it is known in the art to produce a silicone emulsion that is delivered by pumps with different pressure differences (see page 6, line 28-29). It would have been obvious to one having ordinary skill in the art at the time the invention was made to use pumps to deliver a continuous stream of pressure to the microchannels to produce microdroplets .

65. Regarding claim 18, the references Higuchi and Klinksiek disclose the claimed invention except for manipulating the flow rate of the first solution to control the rate of

the droplet formation. Nisisako teaches that it is known to change the flow speed of the continuous phase to change the droplet size. The droplet size decrease as the average velocity increases of the continuous phase (see page 958, section 3.1). It would have been obvious to one having ordinary skill in that art at the time the invention was made to change the flow rate of the dispersion phase with an aqueous solution to change the size of the droplet, rather than the continuous phase flow rate.

66. Regarding claims 19-20, the references Higuchi and Klinksiek disclose the claimed invention except for increasing the flow rate of the second solution to decrease the size of the droplets formed. Nisisako teaches that it is known in the art that at a given dispersed phase, the droplet size decreases as the average velocity (flow speed) increase of the continuous phase flow (see page 958, section 3.1 and Figure 3). In Figure 3, the graph shows the effect on the droplet size of the continuous phase flow, either increasing or decreasing. As the size of the droplet decreases, the continuous phase flow speed increases. The continuous phase flow content was high and oleic sunflower oil was used as the oil phase. It would have been obvious to one having ordinary skill in the art at the time the invention was made to change the flow speed of the continuous phase flow at a constant dispersed phase to change the droplet size produced.

67. Claims 31-33 is rejected under 35 U.S.C. 103(a) as being unpatentable over Higuchi, and further in view of USP 6,211,654 to Quake (herein referred “Quake”).

68. Regarding claim 31,the reference Higuchi discloses the claimed invention except for processing the droplet. Higuchi discloses a process and apparatus for rapidly

producing an emulsion and microcapsules in a simple manner. The microcapsules include a step of feeding a shell-forming phase to a continuous phase. A dispersion phase is ejected toward the junction of the flow of a first and second continuous phase flowing in the microchannels. The dispersion phase joins the flows of the first and second continuous phase and produces a microdroplet (see Figure 6, abstract, page 1 [0007], page 4 [0060-0061]). Quake discloses a device for analyzing and sorting polynucleotides by size (see abstract and column 1, line 14-17). It would have been obvious to one having ordinary skill in the art at the time the invention was made to produce a microdroplet from the sandwiching of three streams and process the droplet formed for analyzing purposes.

69. Regarding claims 32-33, the reference Higuchi discloses the claimed invention except for processing the droplet generated from the first stream. Quake discloses a microfabricated device for analyzing and sorting the polynucleotide by size (see abstract and column 1, line 14-17). It would have been obvious to one having ordinary skill in the art at the time the invention was made to produce microdroplets by sheath flow then analyze and sort the particles by size to determine different sizes produced from the sandwiching of three input streams.

70. Claims 34-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Higuchi and Quake as applied to claim 31 above, and further in view of USP 6,733,172 to Lee (herein referred “Lee”).

71. Regarding claims 34-36, the references Higuchi and Quake disclose the claimed invention except for splitting the droplets into equal or unequal sizes. Lee discloses a magnetohydrodynamic fluidic system that splits droplets in a MHD microfluidic channel (see column 5, lines 65-66). An initial droplet in the droplet splitter channel is moved along the microfluidic channel by utilizing a sequential set of MHD pumps. The pumps provide a MHD micropump in which the Lorentz force is used to propel the droplet along the microchannel. The droplet is stretched into separate droplets by control of the MHD pumps that are selectively activated to stretch the droplet until the components are separate (see column 6, lines 1-6 and 21-31). Since the controls are selectively activated the droplet splitter is capable of producing equal and unequal sized droplets by activating particular pumps to stretch and separate the components. It would have been obvious to one having ordinary skill in the art at the time the invention was made to split a droplet into smaller components for minuscule sampling or testing of droplets.

72. Regarding claim 37, the reference Higuchi and Quake disclose the claimed invention except for the processing comprises of fusing two or more droplets together. Lee discloses a droplet mixer where one droplet is stretched into two component sections and a second droplet is moved into contact with the droplet and by use of MHD pumps the two droplets are combine to form a mixed material (see column 6, lines 43-56, Figure 3A-B). It would have been obvious to one having ordinary skill in the art at the time the invention was made to fuse two droplets together to form a larger droplet either mixing materials or creating a larger droplet for analysis.

73. Claims 34-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Higuchi and Quake as applied to claim 31 above, and further in view of WO 2004/002327 to Stone et al. (submitted on the Information Disclosure Statement on 10 September 2004, herein referred "Stone").

74. Regarding claims 34-36, the references Higuchi and Quake disclose the claimed invention except for splitting the droplets into equal and unequal sizes. Stone discloses a microfluidic device and method for forming a discontinuous section of similar or dissimilar size in a fluid provided (see abstract). In a plurality of microchannels, each carrying a plurality of subject droplet are moved along the channel toward a different arrangement of obstruction to form a variety of different sized droplets. As the droplet flows through the channel, it is free from obstruction and its flow is unaffected. In the different channels, depending on the arrangement of the obstructions, the sizes of the new droplets downstream of the obstructions can be of equal/uniform size or unequal sizes. This occurs when the larger droplet comes in contact with the obstruction(s) (see page 19, lines 15-33; Figure 6). It would have been obvious to one having ordinary skill in the art at the time the invention was made to incorporate obstructions in different patterns in the outlet channels of the newly formed microdroplet emulsions to split or form discontinuous sections of similar or dissimilar fluid particles.

75. Claim 38 is rejected under 35 U.S.C. 103(a) as being unpatentable over Higuchi and Klinksiek, and further in view of USP 6,540,895 to Spence (herein referred "Spence").

76. Regarding claim 38, the reference Higuchi and Klinksiek disclose the claimed invention except for a droplet processor. Higuchi discloses a process and apparatus for rapidly producing an emulsion and microcapsules in a simple manner. The microcapsules include a step of feeding a shell-forming phase to a continuous phase. A dispersion phase is ejected toward the junction of the flow of a first and second continuous phase flowing in the microchannels. The dispersion phase joins the flows of the first and second continuous phase at a junction and produces a microdroplet (see Figure 6, abstract, page 1 [0007], page 4 [0060-0061]). Klinksiek discloses a device for producing a silicone and/or silane emulsion where the components are fed by the means of two pumps, one for the two aqueous phases and one for the silicone oil. The dispersion of the emulsion that is formed is dispersed in a downstream jet (see page 6, lines 21-29). Spence discloses a microfacricated device for sorting cells based on a desired characteristic such as reporter labeled cells and can be sorted by the presence or level of the reporter on the cell. Along the main channel of the sample inlet there is a detection region that is in communication with processor (computers and software) to detect a signal representative of cell characteristics (see abstract and column 8, lines 27-29 and 36-37). It would have been obvious to one having ordinary skill in the art at the time the invention was made to use a detection system that detects cell characteristics with a computer, where data can be stored and processed, to be used in the analysis of microdroplets that are produced from the multiple input microchannels with the aid of pumps.

77. Claim 39 is rejected under 35 U.S.C. 103(a) as being unpatentable over Higuchi and Klinksiek as applied to claim 38 above, and further in view of Lee and USP 2002/0058332 to Quake and Thorsen (submitted on the Information Disclosure Statement on 10 September 2004, herein referred “Thorsen”).

78. The references Higuchi and Klinksiek disclose the claimed invention except for where the droplet splitter has two or more daughter channels in communication with the splitter input channel. Thorsen discloses a microfluidic device for analyzing and/or sorting biological materials with a main channel and branch channels (see page 8 [0077]). Lee discloses a device where there are MHD pumps located along the microchannels that are capable of moving the droplet in the microchannel to the desired location or splitting the droplet (see column 6, lines 21-24 and Figure 2B). It would have been obvious to one having ordinary skill in that art at the time the invention was made to combine the microfluidic device of Thorsen and the MHD pumps of Lee along the walls of the microchannels to move the droplets to desired locations along the channels and split the droplet at the precise location to allow each split droplet flow down each daughter/branch channel.

79. Claim 40 is rejected under 35 U.S.C. 103(a) as being unpatentable over Higuchi and Klinksiek as applied to claim 38 above, and further in view of Quake.

80. Regarding claim 40, the reference Higuchi and Klinksiek disclose the claimed invention except for droplet processor that comprises of droplet sorter. Quake discloses a microfabricated device that analyzes and sorts single polynucleotides by size. The

device has a solution inlet that has a plurality of branch channels that are in fluid communication and branch out from the discrimination region. The flow of molecules is maintained through the device via a pump of pressure differential and a directing means comprising of a valve structure at the branch point effective to permit the molecule to enter only one of the branches (see column 2, lines 49-51, 63-67, column 7, line 8, 14-20 and Figure 1). It would have been obvious to one having ordinary skill in that art at the time the invention was made to sort the droplets that are formed via an input channel and daughter channels that are regulated via pumps to maintain a flow and a pressure gradient to avoid the droplets in the device from being stagnant.

81. Claim 41 is rejected under 35 U.S.C. 103(a) as being unpatentable over Higuchi and Quake as applied to claim 38 above, and further in view of Lee.

82. Regarding claim 41, the references Higuchi and Quake disclose the claimed invention except for the droplet processor comprises of a droplet fuser. Lee discloses a magnetohydrodynamic fluidic system that mixes droplets. The droplet mixer disclosed is enhanced by stretching one droplet to engulf another. A first droplet is introduced into a microchannel and moved along the channel by a set a MHD pumps and stretched into two separate component sections. A second droplet is introduced into another microchannel and moved toward the first stretched droplet by use of the MHD pumps and moved into contact with the first droplet between the two separate component sections of the droplet. The set of MHD pumps are used to combine the droplet to form a mixed material (see column 6, lines 43-56; Figures 3A-B). It would have been

obvious to one having ordinary skill in the art at the time the invention was made to fuse together two microparticles in a device to form a larger particle with either different or identical concentrations to produce a well-mixed particle for analysis.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHRISTINE T. MUI whose telephone number is (571)270-3243. The examiner can normally be reached on Monday-Thursday 7-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Walter Griffin can be reached on (571) 272-1447. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

CTM
/Walter D. Griffin/
Supervisory Patent Examiner, Art Unit 1797